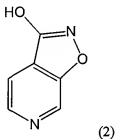


**AMENDMENTS TO THE CLAIMS**

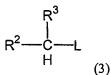
The following listing of claims replaces all prior listings of claims presented in the application.

1 (Currently amended). A method of preparing THIP comprising the steps:

a) reacting a compound of formula (2)



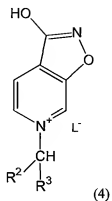
with an alkylating agent of formula (3)



wherein  $R^2$  and  $R^3$  are independently selected from H,  $C_{1-12}$  alkyl,  $C_{2-12}$  alkenyl,  $C_{3-8}$  cycloalkyl,  $C_{3-8}$  cycloalkenyl, acyl, aryl, or heteroaryl, optionally substituted with a  $C_{1-12}$  alkyl,  $C_{1-12}$  alkoxy, or aryl, and

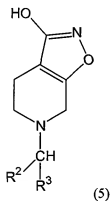
L is a leaving group,

to obtain a quaternary salt of formula (4)



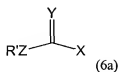
wherein L, R<sup>2</sup> and R<sup>3</sup> are as defined above,

b) reacting the quarternary salt of formula (4) with a mild reducing agent to obtain a compound of formula (5)



wherein R<sup>2</sup> and R<sup>3</sup> are as defined above,

c) reacting a compound of formula (5) with a reagent of formula (6a)



wherein R' is C<sub>1-12</sub> alkyl, C<sub>2-12</sub> alkenyl, C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl, acyl, or aryl optionally substituted with one or more C<sub>1-12</sub> alkyl, C<sub>1-12</sub> alkoxy, or aryl,

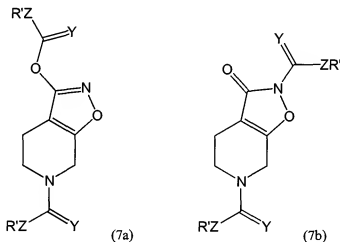
X is a leaving group,

Y is O or S,

Z is O, S or C<sub>1-6</sub> alkyl,

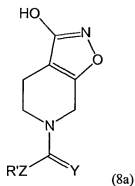
optionally followed by reaction with a nucleophile,

to obtain a mixture of a compound of formula (7a) and a compound of formula (7b)



wherein Y, Z, and R' are as defined above,

d) reacting the mixture of (7a) and (7b) with a nucleophile, followed by acidification, to obtain a compound of formula (8a)



wherein Y, Z, and R' are as defined above, and

e) reacting a compound of formula (8a) with an acid to obtain THIP as an acid addition salt.

2 (Currently amended). The method of claim 1 wherein step a) is carried out in a polar solvent, ~~such as NMP.~~

3 (Currently amended). The method of claim 1 ~~any one of claims 1-2, step a)~~, wherein in the alkylating agent of formula (3), R<sup>2</sup> and R<sup>3</sup> are independently selected from H, methyl, ethyl, allyl, phenacyl, phenyl, or methoxyphenyl and

L is selected from Br, Cl, I, OMs, or OTs.

4 (Original). The method of claim 3, wherein the alkylating agent of formula (3) is selected from MeI, EtI, BzBr, *p*-CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Br, allylBr, and the corresponding mesylates (OMs) and tosylates (OTs).

5 (Currently amended). The method of claim 1 ~~any one of claims 1-4~~ wherein the reduction in step b) is carried out in alcohol and water, ~~such as aqueous ethanol.~~

6 (Currently amended). The method of claim 1 ~~any one of claims 1-5~~ wherein the mild reducing agent in step b) is LiBH<sub>4</sub> or NaBH<sub>4</sub>.

7 (Currently amended). The method of claim 1 ~~any one of claims 1-6, step e~~, wherein in the reagent of formula (6a), R' is C<sub>1-12</sub> alkyl, C[[i]]<sub>2-12</sub> alkenyl, C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl, acyl, or aryl optionally substituted with a C<sub>1-12</sub> alkyl, C<sub>1-12</sub> alkoxy, or aryl,

X is selected from Cl, Br, I,

Y is O[[,]] or S<sub>x</sub>,

Z is O[[,]] or S.

8 (Currently amended). The method of claim 7, ~~step e~~, wherein the reagent of formula (6a) is selected from C<sub>1-12</sub> alkyl chloroformate, ~~such as methyl chloroformate, ethyl chloroformate, or ethyl chlorothiоlformate.~~

9 (Currently amended). The method of claim 1, ~~step e~~, wherein a compound of formula (5) is first protected as a carbonate or carbamate, ~~such as a t-butyl or 2,2,2-trichloroethyl carbonate/carbamate,~~ and then reacted with the reagent of formula (6a) in step c.

10 (Currently amended). The method of claim 1 ~~any one of claims 1-9, step d~~, wherein the nucleophile in step d is a soft nucleophile, ~~such as aqueous ammonia, an amine or diamine (such as methylamine, ethylenediamine), thiols, thiolates, sulfides,~~ in an aqueous or organic solution.

11 (Currently amended). The method of claim 1 ~~any one of claims 1-10, step d~~, wherein the reaction with a nucleophile in step d is followed by acidification by adjusting pH to  $\leq 5$ .

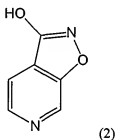
12 (Currently amended). The method of claim 1 ~~any one of claims 1-11,~~ wherein in step d, after reaction with the nucleophile in an aqueous solution is followed by separating the aqueous phase, followed by acidification with an aqueous acid, and extraction into an organic phase.

13 (Currently amended). The method of ~~claim 1~~ any one of claims 1-12, wherein, prior to step e), a compound of formula (8a) or a salt thereof is purified by a process of extraction from one phase to another.

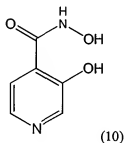
14 (Currently amended). The method of ~~claim 1~~ any one of claims 1-13, wherein in step d) a compound of formula (8a) is obtained in high purity, ~~more than 98%, preferably greater than 99%~~ according to HPLC.

15 (Currently amended). The method of ~~claim 1~~ any one of claims 1-14, wherein step e) is carried out using a mineral acid.

16 (Currently amended). A method of preparing a compound of formula (2)

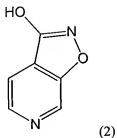


comprising reacting the compound of formula (10)



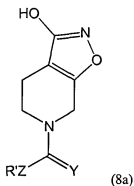
with a dehydrating agent, to obtain the compound of formula (2).

17 (Original). A compound of formula (2)



or a salt thereof.

18 (Currently amended). A method of preparing THIP comprising reacting a compound of formula (8a) or a salt thereof



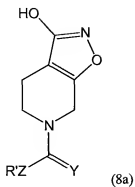
wherein R' is C<sub>1-12</sub> alkyl, C<sub>2-12</sub> alkenyl, C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl, acyl, or aryl optionally substituted with one or more C<sub>1-12</sub> alkyl, C<sub>1-12</sub> alkoxy, or aryl,

Y is O or S, and

Z is O, S or C<sub>1-6</sub> alkylene,

with an acid, typically a mineral acid, to obtain THIP as an acid addition salt.

19 (Currently amended). A compound of formula (8a)



wherein R' is C<sub>1-12</sub> alkyl, C[[1]]<sub>2-12</sub> alkenyl, C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl, acyl, or aryl optionally substituted with one or more C<sub>1-12</sub> alkyl, C<sub>1-12</sub> alkoxy, or aryl,

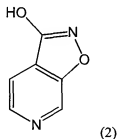
Y is O or S,

Z is O, S or C<sub>1-6</sub> alkyl, or

a salt thereof.

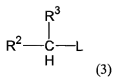
20 (Currently amended). A method of preparing THIP comprising the steps:

a) reacting a compound of formula (2)



with an alkylating agent of formula (3)

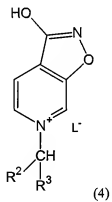




wherein  $R^2$  and  $R^3$  are independently selected from  $H$ ,  $C_{1-12}$  alkyl,  $C_{2-12}$  alkenyl,  $C_{3-8}$  cycloalkyl,  $C_{3-8}$  cycloalkenyl, acyl, aryl, or heteroaryl, optionally substituted with a  $C_{1-12}$  alkyl,  $C_{1-12}$  alkoxy, or aryl, and

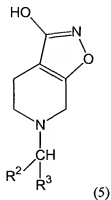
$L$  is a leaving group,

to obtain a quarternary salt of formula (4)



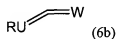
wherein  $L$ ,  $R^2$  and  $R^3$  are as defined above,

b) reacting the quarternary salt of formula (4) with a mild reducing agent to obtain a compound of formula (5)



wherein  $R^2$  and  $R^3$  are as defined above,

c2) reacting a compound of formula (5) with a reagent of formula (6b)



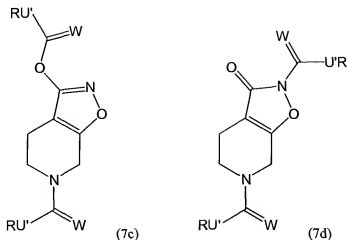
wherein R is  $C_{1-12}$  alkyl,  $C_{2-12}$  alkenyl,  $C_{3-8}$  cycloalkyl,  $C_{3-8}$  cycloalkenyl, acyl, or aryl optionally substituted with one or more  $C_{1-12}$  alkyl,  $C_{1-12}$  alkoxy, or aryl,

U is N or  $CR^1$ , wherein  $R^1$  is H[,], or R,

W is O, S or  $NR^4$ , wherein  $R^4$  is H[,], or R,

optionally followed by reaction with a nucleophile,

to obtain a mixture of a compound of formula (7c) and a compound of formula (7d)

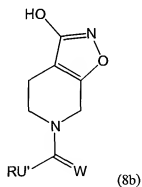


wherein R is C<sub>1-12</sub> alkyl, C<sub>2-12</sub> alkenyl, C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl, acyl, or aryl optionally substituted with one or more C<sub>1-12</sub> alkyl, C<sub>1-12</sub> alkoxy, or aryl,

U' is N or CR<sup>1</sup>, wherein R<sup>1</sup> is H[,.] or R,

W is O, S or NR<sup>4</sup>, wherein R<sup>4</sup> is H[,.] or R,

d2) reacting the mixture of (7c) and (7d) with a nucleophile, followed by acidification, to obtain a compound of formula (8b)



wherein W, U', and R are as defined above,

e2) reacting a compound of formula (8b) with an acid to obtain THIP as an acid addition salt.

21 (Currently amended). The method of claim 20 wherein step a) is carried out in a polar solvent, ~~such as NMP~~.

22 (Currently amended). The method of claim 20 ~~any one of claims 20-21, step a)~~, wherein in the alkylating agent of formula (3), R<sup>2</sup> and R<sup>3</sup> are independently selected from H, methyl, ethyl, allyl, phenacyl, phenyl, or methoxyphenyl and

L is selected from Br, Cl, I, OM, or OTs.

23 (Original). The method of claim 22, wherein the alkylating agent of formula (3) is selected from MeI, EtI, BzBr, *p*-CH<sub>3</sub>OC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>Br, allylBr, and the corresponding mesylates (OMs) and tosylates (OTs).

24 (Currently amended). The method of claim 20 ~~any one of claims 20-23~~ wherein the reduction in step b) is carried out in alcohol and water, ~~such as aqueous ethanol~~.

25 (Currently amended). The method of claim 20 ~~any one of claims 20-24~~ wherein the mild reducing agent in step b) is LiBH<sub>4</sub> or NaBH<sub>4</sub>.

26 (Currently amended). The method of claim 20 ~~any one of claims 20-25, step e2)~~, wherein in the reagent of formula (6b), R is C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl, acyl, or phenyl optionally substituted with a C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, or phenyl,

U is N or CR<sup>1</sup>, wherein R<sup>1</sup> is H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl, acyl, or phenyl optionally substituted with a C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, or phenyl,

W is O, S or NR<sup>4</sup>, wherein R<sup>4</sup> is H, C<sub>1-6</sub> alkyl, C<sub>2-6</sub> alkenyl, C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl, acyl, or phenyl optionally substituted with a C<sub>1-6</sub> alkyl, C<sub>1-6</sub> alkoxy, or phenyl.

27 (Currently amended). The method of claim 20 ~~any one of claims 20-26, step e2~~, wherein the nucleophile is selected from Cl<sup>-</sup>, Br<sup>-</sup>, I<sup>-</sup>, or NC-S<sup>-</sup>.

28 (Currently amended). The method of claim 26 ~~any one of claims 26-27, step e2~~, wherein the reagent of formula (6b) is selected from an isocyanate, ~~such as isopropyl isocyanate or phenyl isocyanate, or an isothiocyanate, such as phenyl isothiocyanate, or a ketene.~~

29 (Currently amended). The method of claim 20, ~~step e2~~, wherein a compound of formula (5) is first protected as a carbonate or carbamate, ~~such as a *t*-butyl or 2,2,2-trichloroethyl carbonate/carbamate,~~ and then reacted with the reagent of formula (6b) in step c2.

30 (Currently amended). The method of claim 20 ~~any one of claims 20-29, step d2~~, wherein the nucleophile [,] in step d2 is a soft nucleophile, ~~such as aqueous ammonia, an amine or diamine (such as methylamine, ethylenediamine), thiols, thiolates, sulfides, in an aqueous or organic solution.~~

31 (Currently amended). The method of claim 20 ~~any one of claims 20-30, step d2~~, wherein the reaction with a nucleophile in step d2 is followed by acidification by adjusting pH to  $\leq$ .

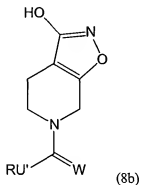
32 (Currently amended). The method of claim 20 ~~any one of claims 20-31, wherein in step d2~~, after reaction with the nucleophile in an aqueous solution is followed by separating the aqueous phase, followed by acidification with an aqueous acid, and extraction into an organic phase.

33 (Currently amended). The method of claim 20 ~~any one of claims 20-32, wherein, prior to step e2~~, a compound of formula (8b) or a salt thereof is purified by the process of extraction from one phase to another.

34 (Currently amended). The method of claim 20 ~~any one of claims 20-33, wherein in step d2~~, a compound of formula (8b) is obtained in high purity, ~~more than 98%, preferably greater than 99% according to HPLC.~~

35 (Currently amended). The method of claim 20 ~~any one of claims 20-34~~, wherein step e2) is carried out using a mineral acid.

36 (Currently amended). A method of preparing THIP comprising reacting a compound of formula (8b) or a salt thereof



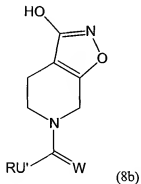
wherein, R is C<sub>1-12</sub> alkyl, C<sub>2-12</sub> alkenyl, C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl, acyl, or aryl optionally substituted with one or more C<sub>1-12</sub> alkyl, C<sub>1-12</sub> alkoxy, or aryl,

U' is NH or CHR<sup>1</sup>, wherein R<sup>1</sup> is H[,], or R,

W is O, S or NR<sup>4</sup>, wherein R<sup>4</sup> is H[,], or R,

with an acid, typically a mineral acid, to obtain THIP as an acid addition salt.

37 (Currently amended). A compound of formula (8b)



wherein[[,] R is C<sub>1-12</sub> alkyl, C<sub>2-12</sub> alkenyl, C<sub>3-8</sub> cycloalkyl, C<sub>3-8</sub> cycloalkenyl, acyl, or aryl optionally substituted with one or more C<sub>1-12</sub> alkyl, C<sub>1-12</sub> alkoxy, or aryl,

U' is NH or CHR<sup>1</sup>, wherein R<sup>1</sup> is H[[,] or R,

W is O, S or NR<sup>4</sup>, wherein R<sup>4</sup> is H[[,] or R, or a salt thereof.